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(54) Title: B-CELL CHRONIC LYMPHOCYTIC LEUKAEMIA

(57) Abstract: The present invention relates to materials and methods for the diagnosis and treatment of B-cell chronic lymphocytic leukaemia (BCLL). The present invention relates to a method of treating BCLL in an individual comprising modulating the expression of the CLLD8 and/or the NY-REN-34 gene.

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B-CELL CHRONIC LYMPHOCYTIC LEUKAEMIA

The present invention relates to materials and methods for the diagnosis and treatment of B-cell chronic lymphocytic leukaemia (BCLL).

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Chronic lymphocytic leukaemia (CLL) is a disorder of morphologically mature immunologically less mature lymphocytes and is manifested by progressive accumulation of these cells in the blood, bone marrow, and lymphatic tissues. There is no curative therapy, and the overall 5-year survival is approximately 60% depending upon the stage of disease.

CLL occurs primarily in middle-aged and elderly individuals, with increasing frequency in successive decades of life. The clinical course of this disease progresses from an indolent lymphocytosis without other evident disease to one of generalised lymphatic enlargement with concomitant pancytopenia. Complications of pancytopenia, including haemorrhage and infection, represent a major cause of death in these patients. Immunological aberrations, including Coombs-positive haemolytic anaemia, immune thrombocytopenia, and depressed immunoglobulin levels may all complicate the management of CLL.

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Understanding the molecular basis for disease, by sequencing the human genome and the genetic elements underlying such conditions will enable the identification of those individuals at greatest risk of disease, and enable the development of effective treatments for disease. This will allow the better matching of treatment and disease, and enable the production of new and improved targets for drugs. Screening and treatment of disease may also be better targeted to those in need, thus increasing the cost-effectiveness of health-care provision.

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The present invention aims to overcome or ameliorate previous limitations in the art by providing means and methods for the detection and treatment of individuals having, or being susceptible to BCLL.

In a first aspect of the invention, there is provided a method of treating BCLL in an individual, the method comprising modulating the expression of the CLLD8 and/or the NY-REN-34 gene. Preferably, the method modulates the production of a gene product of the CLLD8 and/or the NY-REN-34 gene. The gene product may be a composite of CLLD8 and/or NY-REN-34. The term "gene product" includes both mRNA and polypeptide sequences derived either from genomic DNA or from isolated or recombinant cDNA coding for sequences the CLLD8 and/or the NY-REN-34 gene. The gene NY-REN-34 is also known as ANGE.

In the present invention, CLLD8 is the gene encoded by nucleotides 294727-309803 of bA103J18.03548 (Figure 1). NY-REN-34 is the gene encoded by nucleotides 313649-346509 of bA103J18.03548 (Figure 1). References to the CLLD8 or NY-REN-34 genes in the present application include variant sequences showing 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% and 100% homology with the NY-REN-34 gene of Figure 1, and preferably sharing one or more functional characteristics with the CLLD8 or NY-REN-34 genes respectively.

There is also provided an isolated or recombinant polynucleotide sequence encoding a protein having the domain structure Pre-SET-SET-Post-SET-PHD-PHD. Preferably, the domain structure is CpGBD- Pre-SET-SET-Post-SET-PHD-PHD. SET and PHD domains will be known to persons skilled in the art.

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Preferably, the CLLD8 and/or the NY-REN-34 genes encode a single gene product comprising both CLLD8 and NY-REN-34. This composite gene product is produced as a splice product of the CLLD8 gene, under control of the CLLD8 promoter, and comprises the NY-REN-34 gene product. This composite CLLD8-NY-REN-34 gene product results from splicing together of the CLLD8 and NY-REN-34 genes and is shown to be involved in BCLL.

By the terms "CLLD8" and "NY-REN-34" are meant either the complete gene product, or parts thereof. Parts of the gene products are preferably splice variants, and preferably include at least one exon. Thus, the single gene product includes at least one exon of both CLLD8 and NY-REN-34.

In particular, the first aspect may be achieved by modulating the activity of a regulatory element e.g. the CLLD8 promoter, or modulating the splicing of the CLLD8 and/or NY-REN-34 genes. By modulating or influencing is meant inhibiting, enhancing or otherwise altering the expression.

In a second aspect of the invention, there is provided a polynucleotide sequence or a gene product of the CLLD8 and/or NY-REN-34 gene for use in the diagnosis or treatment of individuals having BCLL.

In a third aspect of the invention, there is provided the use of a polynucleotide sequence or a gene product of the CLLD8 and/or NY-REN-34 gene in the manufacture of a diagnostic for diagnosis of individuals having BCLL, or in the manufacture of a medicament for treatment of individuals having BCLL.

In the present invention, the diagnosis of individuals having BCLL includes the determination of whether an individual is predisposed or susceptible to BCLL.

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In addition, the treatment of individuals having BCLL includes prevention of BCLL, and prophylactic and therapeutic measures.

In a fourth aspect of the invention, there is provided an agent capable of influencing expression of a polynucleotide sequence of the CLLD8 and/or NY-REN-34 gene, or production of a gene product sequence of the CLLD8 and/or NY-REN-34 gene, for use in a method of treating BCLL. Preferably, the agent is capable of influencing the activity of the CLLD8 gene promoter and/or influencing RNA splicing of the CLLD8 gene. Examples of agents according to the fourth aspect include but are not limited to proteins, such as transcription factors, which may bind to the CLLD8 promoter or splice sites; antibodies or binding partners; ribozymes; and polynucleotide sequences.

Preferred agents for use in the fourth aspect include polynucleotide sequences which are complementary to the polynucleotide sequence of the CLLD8 and/or NY-REN-34 gene or a gene product sequence of the CLLD8 and/or NY-REN-34 gene. Sequence complementarity can be determined using conventional techniques available in the art. Preferred complementary, or antisense, sequences are those which hybridise under stringent conditions.

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In relation to the present invention, "stringent conditions" refers to the washing conditions used in a hybridisation protocol. In general, the washing conditions should be a combination of temperature and salt concentration so that the denaturation temperature is approximately 5 to 20% below the calculated T_m of the nucleic acid under study. The T_m of a nucleic acid probe of 20 bases or less is calculated under standard conditions (1M NaC1) as [4°C x (G+C) + 2°C x (A+T)], according to Wallace rules for short oligonucleotides. For longer DNA fragments, the nearest neighbour method, which combines solid thermodynamics and experimental data may be used, according to the

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principles set out in Breslauer *et al.*, *PNAS* 83: 3746-3750 (1986). The optimum salt and temperature conditions for hybridisation may be readily determined in preliminary experiments in which DNA samples immobilised on filters are hybridised to the probe of interest and then washed under conditions of different stringencies. While the conditions for PCR may differ from the standard conditions, the T_m may be used as a guide for the expected relative stability of the primers. For short primers of approximately 14 nucleotides, low annealing temperatures of around 44°C to 50°C are used. The temperature may be higher depending upon the base composition of the primer sequence used.

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Antisense sequences may be useful as primers in any of the aspects of the present invention.

In a fifth aspect, there is provided the use of an agent as defined above in the manufacture of a medicament for use in treating BCLL.

In a sixth aspect of the invention, there is provided a pharmaceutical composition comprising a polynucleotide sequence, gene product or agent as defined above for use in treating BCLL.

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In a seventh aspect, there is provided a method of diagnosing an individual as having BCLL, or predicting severity of disease in an individual, comprising determining in an individual the presence of a polynucleotide or a gene product sequence of the CLLD8 and/or NY-REN-34 gene. Current diagnostic or prognostic methods are performed on a sample removed from an individual. Preferably, the methods involve obtaining a tissue sample from the individual; preparing from the tissue sample a nucleic acid or protein sample; and analysing the nucleic acid or protein sample for the presence or absence of a particular spice variant. Where nucleic acid is to be analysed, it is preferred

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that an amplification step be performed prior to analysis. A preferred amplification technique is PCR, although any other suitable methods may be employed.

- In an eighth aspect there is provided a polynucleotide sequence or gene product of the CLLD8 and/or the NY-REN-34 gene for use in a screen for an agent which modulates production of a gene product of the CLLD8 and/or the NY-REN-34 gene in BCLL.
- Preferred features for the second and subsequent aspects of the invention are for the first aspect *mutatis mutandis*.

Figure 1 shows the sequence of bA103J18.03548 which includes the sequences of CLLD8 and NY-REN-34.

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Figure 2 shows co-expression of the CLLD8 NY-REN-34 (ANGE) gene complex.

Example

It is of interest that CLLD8 is in close proximity (approximately 4Kb) to NY-REN-34, that NY-REN-34 has an alternate first exon without a promoter, and that high molecular weight bands were observed on Northern Blots of NY-REN-34 (as shown in Figure 2). In order to establish if CLLD8 and NY-REN-34 may on occasion form a single gene product, PCR was performed between CLLD8 and NY-REN-34 exons in placental cDNA. A band was observed, indicating the presence with a gene with the domain structure CpGBD-PreSET-SET-PostSET-PHD-PHD. A similar domain structure has been observed in IL-5 promoter REII-region-binding protein (Garlisi, C. G. et al. *Am J Respir Cell Mol Biol* 24, 90-98. (2001)).

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The coincidence of the BCLL locus to BCLL may be relevant, as B-Cells produce IgE. Mutations associated with BCLL have not been identified in any of the genes mapped to this locus. However the recognition that CLLD8/NY-REN-34 form a single transcript with differential splicing suggests that this gene may cause BCLL.

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CLAIMS

- A method of treating BCLL in an individual comprising modulating the expression of the CLLD8 and/or the NY-REN-34 gene.
 - 2. A method according to claim 1 wherein the production of a gene product of the CLLD8 and/or the NY-REN-34 gene is modulated.
- A method according to claim 1 or claim 2 wherein the activity of a
 CLLD 8 regulatory element is modulated.
 - 4. A method according to claim 3 wherein the regulatory element is a promoter.

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- 5. A method according to claim 1 or claim 2 wherein the splicing of the CLLD8 and/or the NY-REN-34 gene is modulated.
- A polynucleotide sequence or gene product of the CLLD8 and/or the
 NY-REN-34 gene for use in the diagnosis or treatment of individuals having BCLL.
 - 7. Use of the polynucleotide sequence or gene product of the CLLD8 and/or the NY-REN-34 gene in the manufacture of a diagnostic for diagnosis of individuals having BCLL.

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- 8. Use of the polynucleotide sequence or gene product of the CLLD8 and/or the NY-REN-34 gene in the manufacture of a medicament for treatment of individuals having BCLL.
- 9. An agent capable of influencing expression of the polynucleotide or gene product of the CLLD8 and/or the NY-REN-34 gene for use in a method of treating BCLL in an individual.
- 10. An agent according to claim 9 wherein the agent is capable of
 10 influencing the activity of the CLLD8 gene promoter and/or influencing RNA splicing of the CLLD8 gene.
 - 11. Use of an agent according to claim 9 or claim 10 in the manufacture of a medicament for use in treating BCLL.
 - 12. A pharmaceutical composition comprising a polynucleotide sequence or gene product of the CLLD8 and/or the NY-REN-34 gene or an agent according to claim 9 or claim 10 for use in treating BCLL.
- 20 13. A method of diagnosing an individual as having BCLL, or predicting severity of disease in an individual comprising determining in an individual the presence of a polynucleotide sequence or gene product of the CLLD8 and/or the NY-REN-34 gene.
- 25 14. A method according to claim 13 wherein the method comprises:
 - (a) obtaining a sample from an individual;
 - (b) preparing from the tissue sample a nucleic acid or protein sample; and

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- (c) analysing the nucleic acid or protein sample for the presence of a particular splice variant
- 15. A method according to claim 14 wherein an amplification step is5 performed on the nucleic acid sample prior to analysis, e.g. PCR.
 - A polynucleotide sequence or gene product of the CLLD8 and/or the NY-REN-34 gene for use in a screen for an agent which modulates production of a gene product product of the CLLD8 and/or the NY-REN-34 gene in RCLL
- 10 BCLL.

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FIG. 1

bA103j18.03548

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1 gaattottta aaattatta aaattaagag ttataagcaa ttotaattto
  51 atctaatggt tcactgaagg ctgggctagg acctggtgtc taaatttttt
 101 tttaaacgat caaagccttc agagccgagt ggccagtcct ataatcctag
 151 gccactagaa aactgaattt cctgaatttt ctgaaaaagt ttttcaagta
 201 gaaagccttc tgggattttt ttttcttttt ttttttccag tccccacttt
 251 ggatgtagta aggettetaa aggteaagtt atettgaget aagaacettt
 301 agatactttc actttcagct tattccttgt tttttgaggt ctttttatag
 351 gtaaagagaa atcaaaacag cttctatctg gctccgttaa ctacttttat
 401 gttccatcct tgaaattcat ttatgtcagc atctgttaca gtacatagta
 451 tgtagtcatg ttttcttcct ctcatcttat ctggtgtcac ttctgcccta
 501 agtgtgccct agctaagtcc ttaggtcttc ttggtgtatc cctctcttgc
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FIG. 1 CONT'D

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20051 tcattaatgt gggtttttca attagtttta cacacacatg tacacatatt
20101 tacacacatt tgtatataca tttatctttt aattttagag gggttcttat
20151 tttaaagtga ctctggcaag ggctacactc tatttttagc tgaaaagtct
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FIG. 1 CONT'D

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20201 ataaagttaa ttgctctgaa gactaatcac agagacttct agaaccatat
20251 cctagatcat gtacttaaac ctatcatttg ttaaacagca gaactcttct
20301 tgactagtct ttctaataat attgagtttc actgagtcat ttttctgttt
20351 gctcatcaag tttagtgtct cttagcttta agaagagtgc tgactataag
20401 cagggcacag tggctcacac ctataagccc agtgctttgg gagactgaag
20451 tgggaggctc acttaaggcc aggagtattg agaccaacgt gggcaacata
20501 ctgagacctg cctctctaca aaagaaattt tgaatcagct gggcatggca
20551 gcatatgcct gtgtgtgtag ctgcacagga ggctgaggct gcattgagct
20601 atgatogoac cactgttgto caggotgggt gacagagtga gatoccatat
20651 cttagaatac aagagtgctg attttaacct ctttggatgc aaatttcaaa
20701 aattcactga tacttatttc aagtttataa qtggatttta aatatttqtt
20751 gatttttatt aagacaagtg totgcatgat gtaccaaatt aaaaatcaag
20801 tggaacagat attatttata tttgtttcct acagccccca aaatagagaa
20851 agtaaatgat cacatttgtg aaattacatg ggagtgttta cagccaatga
20901 aaggtgatcc agttatttac agtcttcaag ttatgttggg aaaagattca
20951 gaattcaaac aggtatgtac caagatatta atgtgtggat gcatattttt
21001 accettttt aatttttatg tattttcagt gtaagatttg gccatcttta
21051 ccttttaatt cataaatatt tattcagtat atattatgtt ccagagatct
21101 caagattcca aatcttttca gtatgaacta cacttgaaca gattattcat
21151 ttatctgata agtattcatt gaattctgtg ccaggcactc aggatatagc
21201 actgaacaaa aagtcccttg cctccatgga gcttacttac attctggtgg
21251 aaaagaagac actataagca agtaaacatg acaatatatt gtcagatata
21301 agtgtaatgg agaaaaaaca aaattggata aaagaaatag ggagtggagg
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21401 catggcccag aggagatgac tatggagaga agagtgttcc aagaagatac
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21601 atactgtggc ttttactcca cgtgaaatga gaagacagtg gaggattttg
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21701 aaactacagt aggacaaggg cagaactaga aagactaata aggaggcttt
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21851 caagaggttt caaagatagc tttctgataa agcaagaata gcagtgagat
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22001 ccctttttcc tgtaacctta attttgaggg cttttaagct gggttgtttt
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22151 gaaattacaa aagatccaaa gagtcagatt aaatctggca tgcaattgtt
22201 tttctttatt aagccatctg caaattgaca ggataattag atttgaaatg
22251 taatttacag ataagtaggt ttccttctaa ggaggaagca aaattaatat
22301 taaagaaaat ataattgtat tacacgttta aaggaaatag ggattccaca
22351 tttgagtagt atatgaataa ccttaaggct tgtttgaatg acttttcttg
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22501 acatctgaaa tacaaaattg aaaacttgat cccatcatct tccctcccag
22551 tatctcctct ccaacatctt tacttcatca gtgtcataga caccaatatc
22601 atcttggtct ccaagettta aattettaga tgaatttttt tttectatea
22651 actcttaatc agaatttgtt tctaaatcca taaaactaca tcagggcctc
22701 atcacttttt acatgtacat caagagtccc tgtcctactc agctcccttc
22751 agtccttcac acagcctcac gattaggatt ccataaacac tgttttaatg
22801 tcacacact acagtggtcc cttttgaatt aacctaaatt tccaactagt
22851 gtaattaatg tattetteet etttgtacea gatetettat eacceteatg
22901 ccatttgttg aggtttttct ttcttaacct aatactgcca ggctcatgga
22951 atggtatatg aagacacatg gaaagtataa agacaaaaat catctattat
23001 atccataaga caaatacata tttttaattt ttactcaatt tacttcagtg
23051 ttatgtatac aattttacac tactttatca tacaacattc tgttttaagt
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23101 gaatcctttt acaggttgaa gcatcccaaa taaagtccaa aattcaaaat
23151 gttccaccca aaatctgaaa ctttttgagg atcgatatga cactcaaagg
23201 aaatgctcat tggagcattt ccaatttcag atttttgggt ttggaatgct
23251 caactagtaa atatgcaact attccaaaat caaaaaaatt gaaatgcttc
23301 tgqttccaaq catttcttat aagggatacc caacctgtac catctcccaa
23351 acatggatca tttctacatt ctattccctg aaacattatg catccttaga
23401 actaatgtat agtcaccatt ttctttcaga tttatcttaa agcttctttc
23451 agtaagttcc tttatatatt gttatcagca tccacatttt tatttattgc
23501 caataattca ctaatttaat gtccttttat taagtaccta ctatatgcta
23551 gattctggag acagaaaaat gagacagaga tcttacttta ctttgagagc
23601 aaagcaatat gtaaaaattt agatttacat cacaggtaca attgaggcag
23651 ctaaaagtac ttgaaagccc ccatgtgttg gttcttctga cttgtagccc
23701 accaactaac tggagaaact caactgacaa gtcatttaac cctatgaacc
23751 ttggttttct caattacaga atgagtggtg ggaggttgct cattattgga
23801 aatgataget eetacagatt gageagtgae tgeatgetga geactgeget
23851 aagtgcttta acaagcatta gttcatttca tcctcataat tatcatacat
23901 gttaactact agtatgtctg ttatactaag gtagttggtc taaaatcaca
23951 tctggagtgt gaagtggtag agcagacctt ggatgccagg ggtgaacagt
24001 tctagtatat agcttcttat ttatgcctag tgttccatta ttggaacact
24051 aagcttgtgg tagttattta tatctcactg atcaaggtta ttgccaaggt
24101 ctqatttttc acaaaaaaa aatttqcaac ctctqqcata aatqqqttaa
24151 ttactagcac attectetga aaateegtgg aattteatte tttttattte
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24451 agaaaagcaa gaaaatgctt gaggaccgat tttgcttgtt ctctagctgc
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24551 gatcctcgct tttgaaattt ctcttgcccc tatgcaacaa acagataagt
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24701 aacacatttt ctgtccagcc ttcacacgta attcttcctt ctaatatttt
24751 attaacagat ttacaagggt cccgactctt ccttccggta ttccagcctt
24801 cagctgaact gtgaatatcg cttccgtgta tgtgccattc gccagtgcca
24851 agactetetg ggacaccagg acctegtagg tecetacage accaeagtge
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24951 gtggaaagca caaggacccg acgggcactg agtgacgagc agtgtgctgc
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25151 aaaacagtgg catttagcac tggcattgag actatagcac atcatttttg
25201 ccattttcag tgcttatatt gttaggtaga ggctggcact ttattagaat
25251 gcaagccaca aaaatatcaa ttttgttttt tttgttaggg tgggtcttct
25301 ttttttcttt ccctctctt ttttttaaca aatgccttct tatagaaaaa
25351 ctttctaaga ggcaacaatt tagaatggat attttgacga atcggcatga
25401 gtgtaacagt gataacctga tctgtttgtt ttaaagatta ttaccaagtg
25451 aaaaattcag aatgaataga atttacacta acatgctata taaaatgtta
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25551 tgtcttaatt atttggtaag tgggattatg atgagtaact ggaggggctt
25601 agaaacaaaa actggatgaa agagtatgca tgaagaaaag cttctttgat
25651 aaatgtggag ttcttcatta taaatatata ttcatgaatt cacagataag
25701 tacttaaaga acagacagtt tacttggcct aaaaatattt tgatgtttac
25751 tcaaaaagta cctcttcagg tcttgagaac atggaaaaga attgagtgct
25801 tttaaatact ttttagaaag taatcataaa agtaaattga atttcaaacc
25851 tatttqqctt ctqttttqtq aacctttqaa ctatatgtat gtgtataagg
25901 gtatacacat acatatatgg catataacaa gtgtacacat atacacataa
25951 caagtgtaga agtatatatt acatacatac actcactctg tctggtatag
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FIG. 1 CONT'D

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26001 gctaattttg aagaactccc ataagtttct gctgcttctc ccataactgc
26051 tgccaccacc atcagaattc ataatcaaac ctaacctttt tgtttggggc
26101 accaaatctg aagacaaaat taatttgcac cagtaaactt caagctgctt
26151 tetteettga aaactaaacg tttaacgtat aatgtetgtt tggatactgt
26201 tccaaattgt tgattgcatg tggttaatgt tgcattagag cactttgcaa
26251 ttgcataatt cattaatgtt ttgtgagctt gcatttgtga gttattggat
26301 gatcagactg aattttgtca agtatcacat tgtacatctt gcctagatgt
26351 cgatgactgc aagtaataat acagtttata atgaaactat ctacaattct
26401 tgttttagca catctgttat ccgtaaaaca cctgtaacta gcttttttaa
26451 tttattattt gaattttagg atagcgaatc actaattttt agttgctgag
26501 gttggcattt tagtgattat taagcacttc tgtcagtctt tgaaaaaaaga
26551 acgtattttt tgtgctttga agatctctga agaatttctt ttataataga
26601 atgggcatgt attgtaacag ttttatgtca aatgatctgt gctgtagaaa
26651 aacattaacc cttgttcaaa aaagaaatgg ataaacttgg cctttctaag
26701 tggtaagaat gacctgtcac tataatatac tgtatgttta cattttattt
26751 aaatttaatc tcttatgtat agggtgataa ccttccccag aaacaacagt
26801 gattqcqatt qttttctaqa aacttcttta aaqtqccaca tttqqcaqta
26851 caaatgagtc tgagtgtaat agcccagaga tttatatata gttgaatgtc
26901 taaaatggta aaatgtgcca ctgtgtcaag ttacagtggc ttatgttttt
26951 catagtaatt caaatgaact tootattttt gatagtaaat gtoatttaat
27001 agtatacttg ccatttgagc ctcactgcaa aattagtgca gaggagaaaa
27051 caatttttaa tqtaatcttq attttacctc atatactqta cattccaaaa
27101 actctaaact ttttaaagat tatagataca ctaccaaaca tatcacctta
27151 aaattgtata aggctgaatg aacttcatac aaatgaaaaa aatctcataa
27201 aaatacataa actatgtagc aaaagtatct gtaaaatcca tggaaaataa
27251 aagttgtatc attctttttg agatacgttt attgtattca tatatattca
27301 ttatttgcta cctgtttaag aaagtgaaat gttatggtct cccctcttcc
27351 aatgagetta aaacattttt eecaacagta tataaatett caacatgaga
27401 ggatgtatat ttattatata aagcccagta aagaataaaa ttagaagttt
27451 tatectagtg acttgatttt gtgcaactca tgaaatatet taetteettt
27501 ccacatataa agaatacagt gagtctaagg taaacttccc agtgggaaga
27551 aaatccctaa cctctccttg cctttcccac atccctattt tctagtacct
27601 tottteque accaccaqag quecaqaace tteetggtag tggcactget
27651 gggtctgcct tccaccagaa aatccaacat tctctcactc atcccccatt
27701 aaaatttcca tcccaagaac ttcctcctgg ggatggacac tcagtgcctt
27751 ttttttttc ttttttaat gggtaagcta gtaaatttta tgttataaat
27801 attttaccac cataaaaaaa tcattgaaaa attcactgaa gaagccaata
27851 tggaaagagg agaactcaat gtttaaaata aagccaactt tttttttta
27901 ttcaagaggt aagtacatag cttcaagctc aaggtctagg ttgaggacaa
27951 tcatgagtcc tattaaagga caaccagttt aaagaacact gtcaggcaag
28001 ctaccacgta gctctccttc actccaggct tagctgttcc agacttccca
28051 gtactgatga aggatcatgt ttttgttcag ctttgcccag tgctgtcatt
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28201 ctctatctct gtagaccaat gccaaagaat tgctttctgg attcactgtt
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28351 agecttgcca tggtcacgaa ttaaaagtgt ggtgaccagt cttccaacgc
28401 ctcagttccc tttggcatgt gggaacacct gattcattct ttgtttcatt
28451 ttcctctgac tcggtctgtc tgctcatggc tctgttggcc gttgatgctg
28501 atggctgcct gattattctc tggctcagga gggctatggc cagtcccttc
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28651 gagagcagca agaatagtgc ctcagagcaa aataacttca tgcactcctt
28701 caatatatca ggaagettae teteeteage ttteteatag aatcatettt
28751 tgttggccag gcacggtggc tcatgcctat aatcttagta ctttggaagg
28801 ccgaggtaga caggtcacct gaggtcagta gttcaagacc agcctggtca
28851 atatggtgaa acccctqtct ctactaaaat agaaaaatta gctaggcatg
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FIG. 1 CONT'D

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28901 atgccaggtg cctgtaatcc tagctactcg ggaggctgag acgggagaat
28951 tgcttgaacc caggaaacgg tggttgcagt gagccgagat ttaaaattta
29001 aaaaatgata ataaaaaaaa aaaaaccttt tcttaggggg acctcagctg
29051 ctctcttcca catctccatt ctccaaggcc tcacagacct ttgcaaattt
29101 ctcaggctta agaaatttct taggagaatt tcagaacttt cttcaaactc
29151 ttcttgagtt tgaatttggt aatccatgtc cagataagta aggttgatcc
29201 aatcaaacaa tttcatgttc ttgtggggtg tgagggctcc aagatatgag
29251 ggggttcaaa gtagttggga ggcctagtca gtgaaggacc atgaaaccag
29301 ccacttatag acaaatgtga cttcagacag gactttggac acctggtgaa
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29401 agagacgaca atctgcttcg gttgaaagtg ttcatcaatg ttgtacaggt
29451 ccaggatacc ctccaggctc ctgtcccagg aaagaaccag gtacaggata
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31351 tatgatagca tttattgatt gagtaccacc tgtttgctag gcaatgtgct
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31501 gaaaccctaa tttctttcct cttgaatttc atcccctgat acttttacta
31551 ccattttgag cccacactca atccttaagg ctagcccatc ttaaatatta
31601 atccaaggat gaaaacgcca tttttgccac ttaccgcaac taagacaagc
31651 tgacattttc aaaaatgaat atagctacca tgtggaccaa cctcaaaaac
31701 acactacaat gaaggaagcc agacacagaa agtcacatat tatacaattc
31751 catttgtatt aaatatccag aatqagtaaa tccatagaga cagattagtg
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31901 actctgaggg cactaaatgc cagtaagttt gtcacttcag aatggttaat
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32251 atctcattct taatccttct aggatgacac agaggtctta aagaagaaat
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32851 agectacagg ctgcaggtgg cagtctttgg ggaacatgag ctcagagctg
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32951 ctccccggat gttaccactc ctctcagcct gcggcacgtg cctggtttac
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33051 taggcccaag atatcatgct gacaatctgg aactttacct gaaatttccc
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33201 gagcccagga gttcaagagc agcctgggca atctagggag acccccatct
33251 ctacaaactt catgccttgc tcttatgtgg ggaaaagagt gtaaagcctg
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FIG. 1 CONT'D

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89751 toctaacaag gtttagtotg tocccaggot gaaacagaaa aagtggotto
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89951 gcaaatataa tottatgttt ataacttotg coacttacot tagaaatgag
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FIG. 1 CONT'D

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FIG. 1 CONT'D

SUBSTITUTE SHEET (RULE 26)

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101351 aggcaggaag actaagggga tcttcagggg cagagatggg aaaggaagca
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101401 cccaqttqqq ccagacctc ccggaaatac cctcactcag gcacatgttc

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FIG. 1 CONT'D

SUBSTITUTE SHEET (RULE 26)

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180901 aatggtggtg tgtaaactac tcttgtctta aggagaaaga ctaaatgatg
180951 aaccaaccaa aaataataac aacttttcaa gatataaaca gtgcaataag
181001 acataaagag aaacaacgaa aagttaaaaa gcaqqqqqaq qaagttaaqq
181051 tqtaqaqttc ttattaqttt tctttctqtq catttcttta tqtaattaqt
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181151 gcctcatggt aacctcaaat ataaaaatac aatggataca caaaaaaata
181201 aaaaacaaga aattaaagca tagtgccaga gaaaatcaca ttcattaaaa
181251 ggaagataga aaggaagaga agaaggaaga gatgactaaa aaacaaccag
181301 aaaacaaata acaaaatggc aggaqtaagc ccccacttgt caataataac
181351 attgtatgta aatggactaa agtctgcaat caaaagacat aaagtggcta
181401 cttgggaggc tgaggtgtaa ggatcacctg agcccaggag gtcaatggtt
181451 cagtgagctg tgattgtgct actacactcc agcctggatg acagagtgag
181501 accctgtctc aaaaaaaaaa aaaagaaaag aaaaagaaaa aagacacaga
181551 atggctgaat ggatgaaaaa aaaacaagac ccaaatgatc tgctgcctac
181601 aagaaacaca totoacotat gaagatacac atggactgaa aataaagaca
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181701 gagtagctat acttacatca gacaaaacag atttcaagac aaaaactgta
181751 agaggagaca aagaaagtca ttatataata ataaaggagt cagttcagca
181801 agaggattta acaattgtaa atatatatgc accaaacact agagcaccca
181851 gatatgtaaa gcaaatatta ttagagctaa agtgagagac acatcccaat
181901 acaacaatag cagatcttag acctgggaca tgataacttt taccactgtt
181951 actcaacata atattggaag tcttagctag agcaatcaaa caagagaatg
182001 aaatgaaggg caaatattat tagagctaaa gtgagagaca gatcccaata
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182101 ttcaacataa tattggaagt cttagccaga gcaatcaaac aagagaatga
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182201 cagatgataa aaccttatat ttggaaaaaa ctaaagactc cacaaaaaaa
182251 ctattagaat tgatgaacaa attcaataaa gttgcaggat acaaaaatca
182301 acatacaaaa atcagtagca tttctatatg ctaacagtga acaatctgaa
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182401 atacctagaa attaacttaa ccaaagaagt aaaaaaatct ccataatgaa
182451 aactataaaa aaatggatga aagaaattaa aaaggacatg caaaaaagga
182501 aagatattcc gtgtccatgg attgaaagaa acaatattgt taaaatgttc
182551 atactaccca acgtaatcta caggttcaat gcaatcccta tcaaaatacc
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182601 aatgacatto ttoatogaaa tagaaaaaac catootaaaa tttacatgga
182651 accacaaaaa acccagaata gccaaaacca tcatgagcaa aaagaacaaa
182701 actgaagaaa tcacatgact tgactttgaa ttatactaca gagctatata
182751 gtaaccaaaa cagcatgata ctggcataaa aatagacaca cagaccaatg
182801 gaacagaaca aagaatccag aaacaaatct acacacctac agtgaactca
182851 ttttttacaa aqqtqctgag aacatacatt qaqqqqaaaa qacaqtcttc
182901 aacaaatagt gcagagaaaa ctgaatatcc acatgcagaa gaatgaaatt
182951 agacccctat ctcttgtcac atacagaaat caaatcaaaa tggattaaag
183001 acttatatct aagatctatg aaactatgaa gctactaaaa gaaaatattg
183051 gggaaactct ccaggacatt ggtctgggca gaaacttctt gagcaaaacc
183101 ccacaagcac aggcaatcaa agcaaaaatg gacaaatggg accacatcaa
183151 attgaaaagc ttctgcacag tgaagggtac aatcaacaaa gtgaagagaa
183201 aacctacaga acacaggeet tetatgaaaa ggtgeteaac ateaetgatt
183251 atcagagaaa tgcaaatcaa aactacaacg agatatcctc tcacgacagt
183301 taaaatqcct ttcatqtaaa cqtcaqqtaa caactattqc tqqtqaqqat
183351 qtqqqqaaaa qqaacccctc atatqctqtt qqtaqqaatq taaattaqta
183401 caactactat ggagaataat ttggaggttc ctcaaaaaac tacaaataga
183451 gataccatat gatttagcaa tcctactctt aggtatatgc ccaaaagaaa
183501 ggaaatcagt atatcaaaga gatatctaca ctcccatata tgttgcagta
183551 ttgttcacaa tagccaagat ttggaaacaa cctaaatgtc caaaaacaga
183601 tgagaaaatg cggataaaga aaatgtggta ccctatacac aataaagtac
183651 tattcagtca taaaaaqqaa tgaqattctg tcattgcaac aacatggatg
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183751 acatcagatg ttctcagtta tttgtgggat ctaaaaatta aaacaagtga
183801 actcatgaaa atcaagaata gaagcatggt taccagaggc taggaagggt
183851 agcaggggag tgtgtcaggg tgagatgggg atggttaatg ggtacaaaaa
183901 acaatagaaa caatgaataa gatctagtaa caccaaggat aaatgcttga
183951 gaggatggat acccaatttt ccatgatgtg gttattacac attacatgcc
184001 tgtactaaaa tatctcatat acactaccta ctatgtaccc acaaaaatta
184051 aaaagaaaaa aagagaaaaa agaaataaat aaaaacccat gctctcacga
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184151 ctaaaaatac aaaaattagc taggcttggt ggcacgcacc tataatccca
184201 gctactcagg aggctgaggc aggggaatcg cttcaaccca ggaggcagag
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184401 tagtatgaaa aacaaacaat ctgccaqqca tggtqqctca cacatgtaat
184451 cccagcactt taggaagcta aggcaggcag atcaccagag gtcaggagtt
184501 cgagaccagc ctgaccaacg tggtgaaacc ttgtctctac taaaaataca
184551 aaaattagct gggcgtggtg gtgcatgcct gtaatcccag ctactcggga
184601 agctgagaca caagaattgc ttgagccctg gaatgagctg agattgtgcc
184651 actgaattee ageetgggea acaqaecaag ateetgeete aaacaaacaa
184751 ataatcccag gcaagaaatt actttggaaa gctgaagcag gattacttga
184801 gccaggagtt tgagagtagc ctgggcaaca tagcaagacc ccatctctac
184851 ttaaaaaata aaataaaaat aaacaaaaca gagaaaatgg ctaaaagaca
184901 tgaagacaca ttttaccaaa gaggatatac agatggcaac aagcacataa
184951 aagacgttca acattgttag ccattaggga aatgaaaatc aaaaccacaa
185001 tgaaatatta ttacatgcct atcagaatgg ctaaaataaa aaatagcaac
185051 aacatcaaat gctggcaaga atgaagagaa actgtactca tacattgtag
185101 tggaaatgta aaacagtata gccaatctgg aaaacacttt agcagttcct
185151 gaaacagcta aacatgcagc taaccataac agcaattgcg ctcttggcat
185201 ctatcacaga gaaatgaaaa ctatgttcac acaaaaacca attagtaggt
185251 gaatetteaa tttaaaagaa tacteeaaaa teagttgete teataatttt
185301 aaaacactaa aaaatgttta taggccgggc acggtggctc atgcctgtaa
185351 ttctagcact ttgagaggcc aagcctggag gctcagttga acccaggagt
185401 ttgagaccag tctgggcaac atggtgaaac cccatctcta caaaaaaata
185451 caaaaattag ctgggtgtag tggcacatgc ctatagtctc agctatttgg
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FIG. 1 CONT'D

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185501 qaqqcttatg tgggaggatc acttgagcct agaaggtgta ggtggaaggt

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185551 gtaggttgca ataagctgag atcatgccac tgcactctag cctgggtgac
185601 agcqtqaqac cctqtctcaa aaaaaaaaaa aggttgaatt acataaattt
185651 tatttatact gatgttaaag actatatttg ctgtataaaa aaagatatag
185701 ctqtaaqcat aaattgattt taaaatgaaa gaaatcatct gtttcgttca
185751 aacctttcta gaccctgcag tgtaatattg cagaataaat atcaacctc
185801 tttgaaatgt cataggaaca tgtttttcat acttcccagt gaaatgtcac
185851 aagaacatto catacagcat tocagtagaa atgaagotot goagaactot
185901 atccaacttt tacatagagg aaaacattct tctagttcat tagcaaatgt
185951 gtgcaaaggc aaaggaagcc ccctgtggat aacaaaagca ggttctgcta
186001 ccagggaccg cttcccaaaa cagaggaaag gattagaata gaaaggatta
186051 caqaacactq aaacaqqtac aaqctqqtqa ataatqatct ctacattaca
186101 cgttaatctt tgtagctatc aatttgtcat gccaaatcta actggagtga
186151 aaccttaact atttcaaaac cagttttttg caacccgcag gctgccagat
186201 ctcaagccct ggactcagaa gtggccagaa aaaaaagaca gaaaaaccct
186251 aaaaatatat ttgataataa agaagcaaca tccagaaatg gcccaaaatg
186301 ccaaaaatta gctggcaatt ctaaggttac atacaatgta accaataaga
186351 toccaaacct gaagaagccc ttgtgtttgc tggcaaattc aaaaaagtca
186401 gctttaacat gaaatgctcc ataattattt gctgaatgaa tgaattatat
186451 atatggaagt attaactcaa atcaaataag aaaagagaaa aggagggaag
186501 aaagaggtgg tgaacagcag tcacagcaac cagaatgatt gctgaaaaag
186551 agcatccctc acagatagca tagatgagaa aagggaaatg agaaaagaag
186601 gcggagacta gaaaacaccc acttcaaaac acaagccatt gacttttata
186651 tagaatatat ataaagaatt ctcaaaattc agcaacgaaa ttaaaaaaggg
186701 gcaaaagata tgaataaata cttcataaaa gaagagatat ggtagcaaaa
186751 atgtacatga aaagatgctc aacatcatta gtcattagag aaatccaaat
186801 taaaatcaca atgagatatc acaaaccctt attagaatgg ctaaaacaat
186851 aaaacaaaac aaaaagttga cattccccaa cagccctact cctaggtatt
186901 tatctaagtg aaaggaaaac ctatgttcac actaaatact atacataaat
186951 ggttaacggc agctttattt gtaattgcta gaaactggaa atatgtaaaa
187001 tatcccacaa gtggggaatg gataaatgat ctgtggtcca tccatgcaat
187051 ggactactac tcagcaataa aaagcaacag actcctaata catggcaacg
187101 acatggatga atctcaaatg cgttatgctg acagaagcca ggctcaaaag
187151 gctacatata tatgattctg tttacccaat ctttttgcaa tggtgaaaat
187201 ataaggactg aaaactgatc aatggttgcc agaggccgag gacaggaaaa
187251 ggagatgatt acaaagaggc aaaggagatt ttttttttt tttgagacaa
187301 agtcttgctc tgtcacccag gctgaagtgc agtggcataa tctcgactca
187351 ctgcaacctc cacctgccag gttcaagtga ttctcctgcc tcaacctccc
187401 gagtagctga gactacaggt gcacaccacc acaccggct aatttttgta
187451 tttttagtag agacagggtt tcaccatgtt ggccaggatg gtctcgggct
187501 cctqacctca tqatctqccc acttcggcct cccaaagtgc tgggattaca
187551 ggcgtgagcc accgtgccca gccggcatag gagaattttt tagggtgatg
187601 gaactgttgt tcttcattac agaactgtgc actaaaaagg gtgaatgtta
187651 ctatttataa attgtatcat aatttttaaa aatgaaaatt atagccagtg
187701 aagtcaggga cttctctatt cttgctggtg tgttgcgggg gagttgaggt
187751 gggtgggagc aagtggttgt gctgaatttc agtagcagaa gtggataggc
187801 agaacagtct accgggtgag gggtagccac tgaatggatt agtgagggat
187851 cttgctgggg actaaaattc aaattggact aatttataga tattgggaaa
187901 gatataggga atgaaactac aagctagete aaagttgete teaaaaaaat
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188251 ccagggtgtc atatcaccca aaatggttgt tcccatggta accatgtgag
188301 tggagaagga gggagcattc cccagaaagc agagggagtg ggcagacaca
188351 acactttata cacagcacaa gcagtcttca tccttatgca gattacattc
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188451 acaaacaatt aacaggtttc acatctaatt aagagcctga tgccaaatgc
188501 catttttaat cacccataaa ttatattcct ttataggata aaggccttct
188551 aaagcttata ttcattaagc tttagggcaa tagggtaatg ataacataaa
188601 atgccatttt ctatgacata gtatttccct acctgagatt gtaaattctt
188651 taatttgtcc agtgagggc acaaaatata tacacaatca aataaaatca
188701 agaccaaaca taattaaata aaatcaatgg ctgacacgca tagtaagcat
188751 ttcaaattgt taaatgtata atgtacagtt aaagctggta ttttaaggct
188801 ttatgatttc tgttatattt ttacagtaat aaaaccaaag gtaaagagcc
188901 gtttcactct tattgcccag gcagaagtgc aatggtgcga tcttggctca
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189001 aagtagctag gattacaggt gcatgccacc atggccacgg ctaatttttg
189051 tatttttagt acagataggg ttttgccacg ttggcgaggc tggtctcgaa
189101 ctcctgaatt taggtatccc aaaatgctgg gattacagac gtaagccacc
189151 acgcctggcc aagggccact ttaatcaggt ccagggaata gaaaaagatt
189201 attagaggat aaacatttac aaaatgtagg actacaaaat ggcttaatga
189251 aaagtggaaa agttgatcct ggagtgtttg ttttgctatt ttttttctt
189301 ttgagacagg gtctcattct attacccagg ctggagtgca gtagcacaat
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189801 acatcaaaga gtctaaagct gtgtcttgaa tagtagccaa acctcaaaaa
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190951 atctaagett ttttctttca gtcttttcct tacagacatt gcctagagac
191001 ttcagccttt caaactaaca aaaaagccaa tcaaggtatc ttctaaacaa
191051 aaattcactt tttttctctg taaggaatgt gccattctcc taggttatct
191101 ggcaaaagct gtagtccatc cttaaaataa taatttttcc tttctgttat
191151 caaaacatac cagaaatttt acagtcaaat gactgttctg ctatccaaag
191201 aagcaccagg agaggetatt cacgtactga aatcatataa tcatcacccc
191251 aaagagtttg aattatcttc taaacaattt actgattcct tcagaaaaat
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FIG. 1 CONT'D

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191301 ggctcactgg tatgtcccaa taccttcttt tggtccaatt cttttacctc
191351 tgctttgata tctcattctc attactacat tcattcaaac aattcacaaa
191401 ttaacatgcc actaggtgtg gcaaacacag tcctcgtact caaggtaaca
191451 cagaagtggc tgtcccagtg caagccatga accaagagac atgggggtgg
191501 gggttctgtg tcgctggagt aagtctgaag tcaqaaggaa ttttatcaag
191551 ctgtcagtag cttacataga tactttaggc ttgagaagga gagttgctgc
191601 ctgcaggctg atcatccatg cctccagttc atagagataa catagtacat
191651 ttctataagt aggctaataa tgctaggaat gctggctgcc tccttcctga
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191801 totacaggot agagaaggat aacggotgoa totatggagt atcacattoa
191851 cttataatta tgttctaggt atgtgtcacg tcaattgaat aaataaagtt
191901 aagaattgcc tatcttatta tcacaataac aaatcttcat aatagttttg
191951 aatcatcagt ttaaaaacgt attatatcta gtattttatt ctqqaqqqaa
192001 qqcaaqtata taatacattt tattttaaaa attaaaqtaa tccacaaqaq
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192101 attcaaatgt tcagaaagat acttcttttc tccaaggatt ccagagaata
192151 aaagtttact tgataaaaat gtacaagtct attttaggca attaaatgtc
192201 ttaattccaa aataattttt aaatgaactt cttctcaaaa tttttaattt
192251 atatttgatq tgccacataa aaqaaqqqqa acttgcataa ctgtttctta
192301 cattccactt ttgttatctg agccaatgcc aaagaaagtt ataaggcacc
192351 caaagttttt ctttggtata ctcctcccta actccccaat tcttggaaag
192401 cactttgaac ctatgaggtt ctgtggctgc tcaaagcttc tacaggtcac
192451 tgaacctgac gacatctcat ccctgactca ttcttcaaaa cataaccatc
192501 cttagtcata ttccttctag cactccactg caaattgggt taatctcata
192551 aactaactca agcgtactta tgaattaatg acgacagtag cttaatatgc
192601 tgctgttctc agagaaacaa gcaaaacaac agaaaattta taaaactata
192651 ctactataag aatagggaat cattttccta tttatggtca ctgaccaact
192701 aaatctaaaa aaaatcaagg gttataacaa aaacaaacca gcttacactt
192751 aactttagtt cctgagtttg agaaaaagag gaaatgaaaa aatactacta
192801 cttgacattt gtatacagtt tgcatttata tttagtqtcc ctatataaca
192851 caacatatat atgtatatat ttttatttag tttaatattt aaaacaatgc
192901 agtaagttcg tattattcct attttataga tgagaaaact taagctcaaa
192951 gaggttaagt tactgaccat gaaagagcag agctgggact ctaaacaatt
193001 ctaattccqa gtcaaqtqtq tttttcacta tqccacaqct tctacaaqtq
193051 ttcataatac ctaattttaa actaaataaa agaaacagaa aagtatatac
193101 atacagtaag actatacttt aatttcacat atagctgatt ttaaatctaa
193151 gatggagacc taagatggag agggagagta agcaagccaa gcaagaggaa
193201 aaagaaaaag attctgagca aactgtcgca aagacaaaaa accaaacact
193251 gcatgttctc attcataggt gggaattgaa caatgagaac actgggacac
193301 aggaagggga aaatcacaca ccggggcctg ttgtggggtc gggggagcgg
193351 ggagggatag cataaggaga tatacctaat gtaaatgacg agttaatggg
193401 tacagcacac caacatggca catgtataca tatgtaacaa acctgcacgt
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193501 aaaaaqaaaa aqattatqqq tcaqaaaatq ccaaaqqcaq aqaaaqaqat
193551 agaataagga agggaaagaa agaaaaagac agctgtaact gaaaggatga
193601 gctgaagtct gggcccttcg gggtccccac ttggtcttgc ttctagccac
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193751 ttccacagat ccccaaagcc ctgacctgat cttggtctaa tcacagtaat
193801 cactgtcatt agttttcctt ccacttattc agtgaacaaa actaaaagct
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193901 acctacctga tacgaacaaa attcgtatta tgatagaaac aaagcaacaa
193951 agccaaacca ggacttctgt cgcctcaaca gtcaatgccc aaacttgtct
194001 atgtatccat ttctcactga aaaatcacca cctctgagtt acacaataga
194051 taataaaatq actaqacata ttcaccactt acatttctaa qcttttqttt
194101 tagttagtca gtttattatt taggtaaatt aggtataatt gccttcaaaa
194151 ggagataagt atattactag cacttaacac atttcttaaa tcattggtat
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FIG. 1 CONT'D

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194201 aatatgttca ttaaaagaac tgtctgaatt tgaagctctg aagtaagtga
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261951 tggtccccgg cggaggttac gccttccctc atccccggta gaggcagggc
262001 gggactgttg tggttgagat gaaggctagt aaatggtgaa gtacttcccg
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262151 cactcctcag gtcaggcggg cggcgtagaa aacgcagcgg agccaggtga
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262401 ctgtctgtct cagggtgcag ccttaatgag aggtgattcc taagctgctg
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263651 tgcgcggtgg gtggctcaca tctataatcc cagcactttg gcagatcact
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263751 aaaaaataaa actattactg agtgtgctta ggtggaagta taaattggta
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263851 gaatteettt ttgaacattt atatataett aatttttaaa aattaagtac
263901 acttttacat tcttttacag aattggtacc ttgtagataa agagcacaat
263951 ccagattttg accttgagtt ttttcttgcg tgtcaaggtt atacttataa
264001 aaacagttga atagcttccc gtatttttcc ttcttgaaaq ttcgtatatg
264051 ataaaaattc tccgttcttt gaaagttttg tacaaggaat gttccctcac
264101 tcctctcct ccctactccc gctggagact ttggtacaga gctttcaagt
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264351 tocagtgtat gactgaattg atotgttaat ataaaacatt totttgtoto
264401 ttttattggt cttgttgtta aatcctattt tgtttgatgt gtgctgtata
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264501 atacaacaat qctqcaaqqa aaatctttqt qttttcttqt qcacatqtqc
264551 tatttctcta ggatatatac ctaaaagtgg aattgcttqg ttttaaqttq
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266001 agctagagat ctatcttcat ttgttattat ttattttgtt gcttttttcc
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266201 taaatttctc ctttgatttc ttctgtaaac catatacatt atttgggaaa
266251 tttgattttt taatttccgc aggtagtatg gggtgggggg ttgatttact
266301 acattcagtg actatgctct gtgtaaacag tcttttggaa tttgttgata
266351 attocttttg gtctcataat agtttttgta aatttcatgc ttttcctccc
266401 acaagaagta ttttctgttg ggtgcagggt tctatatatt ttttggatta
266451 agcttgttaa tttgtcattt aaatccttta tactctggtt ttttacccac
266501 tttatctcag ttccttagat ttgttacttc atcaccaaat tgtggatctg
266551 tgcattttcc ttttaatttt gctttatata tttcagagtg atgttatttg
266601 tacataaagg gtcatgaata ttaaatctgg tgaattgttc tgtcagcata
266651 aaatatttgt gtcttttatt gattttcata ttcaactctt atttgatacg
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FIG. 1 CONT'D

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266701 tttcttctta taattgcaga tgtctttttc cagtctcttc gttttcagcc
266751 ttgctgtgac attttgtgta atttaagtgg gtctcttatt ttaaaatatc
266801 atatctgggt tttgcttgcc atccaatctg agagtctgcc ctttaatagg
266851 taattcacct ttattgtgat tattgacata ttttggcctt attcttgtca
266901 ttatttaaca agcttctctt tgtatctttt atatcttatt tttccacctg
266951 ttttttggaa cagagtcttg ctctgttgcc caggctggag tacagtggcg
267001 tgatctcggc tcactgcaac ctctgcctcc caggttcaag caattttcct
267051 ccctcagcct cccaagtagc ccagattaca ggtacacacc accacacca
267101 gctaattttt gtatttttgg tagagatggg atttcgccat gttggccagg
267151 ctggtcttga actcctgacc tcaggtgatc cacccacctc agcctcccaa
267201 agcgctggca tcacttttat ttttaattga ggttagcccc aagttttctt
267251 tgttcatttt tttttaagtt gattaacttt acatttcaca gttcttaaat
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267351 gtaaagaaga agttagcatg cttctacttt gctttctctc atcttgaaac
267401 aatcccttcc atctcctc cagaaaagaa cataatctct catgatatct
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267651 atggaaagat agcttggctg gatatagagt tctgggttca tactgacttt
267701 gctttaacat tttgcatctg acatttctga tgagaaatct cattactagt
267751 ctaatacacc ttccttttag ataatctaca tttttctgga aacatctaag
267801 actttgtgtt tttgatattc tgaagttagt cacggtttgt ctagcgatgt
267851 gtgttaagaa ttttatcctg gttggtactc agtggattca gtttgcttat
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268101 ccaagatagc taactggctt tttttcaaaa ttgtgtgtta tttcatggat
268151 gagatttcct tctttagctc agtctctttc atagtgtagc cttcttcaga
268201 tatttgagga ctctcagttg tgcattaatc tcctctgaga ggattcctgc
268251 ccatcgtttt gctgttgtga ttgtggttgc catcatctct atagcttccc
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268551 tatttatttt agcattattt attatactaa aaattaatct ataaaggaaa
268601 acaatctaaa tatcgaatat agaggtttat attattaatt aatattttta
268651 ttaaaattta attattaaaa tatttaatgt actataatgt atgcgttatt
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268751 ggaggaaaat gcaggaaatg tttttaatga aagattataa aaaattaaat
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269501 gattccagtg atattctgca atcaaagtga tttgataaac ctaattttga
269551 agcattttat atttataagc gacatcaaaa gatgggagaa aaaaatggta
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FIG. 1 CONT'D

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269601 ggttgaagaa cacactgtta cactttatat ctaaaagtat aaaagtatat
269651 agacaatgta agctgatgtg gaattgtcaa ggttttgcat tgcgaggaac
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FIG. 1 CONT'D

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FIG. 1 CONT'D

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FIG. 1 CONT'D

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381851 acctatcaac ctgcatcccc ggttctttca atatggcaac tacatgaatg
381901 ccagagaaca gatgaagatt tcccgattca agatgcaagc aatgcacaaa
381951 qaaaggaaag ccaggtagca tctatgttta gaaaaatgta ccggccgggc
382001 acagtggctc atgcctgtaa tcccagcact ttgggaagcc aaggtgggcg
382051 gatcacgagg tcaggagttc cagaccaacc tggccaatat gatgaaaccc
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382151 gtggtctcag ctactcggga ggttgaggca gaagaatcgc ttgaacccag
382201 qaqatqqaqq ttqaqtqqqc cqaqatcatq ccactqcact ccaqcctgga
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382551 cctgggcgac agagagagac tccgtctcaa aaaaaaaaag aaagaaagaa
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383251 aagtgaggag cgtctctgcc cggccgccca tcgtctggga tgtgaggagc
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384151 gtgtttaact ttcacctgct ttatgtactt cctctcagaa attaagaagc
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385301 ctctaaaaac agccaaagca gcaggtcaag accaagttct ggctccagca
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385451 gatgacaagg atcagcttca gccccaggta tcataccaca aattcaatga
385501 ggattaaacg ccqtcaaatc aqqctattca ttgtcactgc atagccagac
385551 tactggaata acatttggat gtcttgacaa atgtgtgtgc aggtggaggg
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385701 aaaqtctcct tatcatccct ccctgaccct ctcctcaaaq gccaccactg
385751 ttcccagtga tctgtaattc cttctggaaa cagtgctcat ggaagcacta
385801 catgtatqca taggtgtatg tgtatcttta aaaacagaag cacaaatgga
385851 agttttttt ccctacttaa cagtacatcg gggaaatcat tctatattag
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386051 gtattgacat gtcttgtttt atacagaaat ttctaaaata aattcctaaa
386101 aatgaaaatt gctaggtcaa agtctaatag ctattttact gttactagct
386151 attaatattt caaacagtct tctattgaag tagtggccat atataaaatc
386201 accatggatg taggatggca cctgtttaca cacacccttc ccacacagcg
386251 tactctcacg gcatttcagt tttgtttaaa ctggcatttc cctgtgatga
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386351 gctcacacct gtaatcccag cactttggga ggccaaggtg ggcagatcag
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386951 ttaaatgctt ttaaaagttt aaaaataaag gctgggcgca gtagctcacg
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387051 cagcagtttg agaccagcct gggcaacatg gcgaaacccc atttctacaa
387101 aaaatacaaa aaaaaaaggc caggcacggt agctcactcc tgtaatccca
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387201 accagactgg caaacatagt gaaaccacat atttactgaa aatacaaaaa
387251 aaattagcct ggcggtagtg gcgcatgcct gtaatcccag ctacttggga
387301 ggctgaggca ggagaatcac ttgagcccgg gaggcagagg tggctgtgag
387351 ccgagactgc atcactgcac tccttgtctg ggtggcagag tgagagaccc
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387501 gagaggattg cttgaaccca ggaagtcaag gctgcagttg agccgagatc
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388301 aagaagctgg gggatttctt gaacagataa gaacaacaga ggcagtaata
388351 ttqqccaaqc aaqtaattat ccctaqcaag acaatcaagc aaagctaaca
388401 gcaggaaaga agaaacgaat aactatootg aacotgoott gtogtagaca
388451 ctgttaatta ggtagcttcc atacattatt tcatttaatc ttcgtaatac
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FIG. 1 CONT'D

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388501 tcttqtqaqq aggagactqt aaaccatttc tqacaqatqa qqactqaqqc

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388551 tcaaaggtga aatgacgcca aggtcacaca gcagacccct ctaatttttc
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391351 tggtctcaaa ctcccgacct caagtgatcc acctacctcg gcctcccaaa
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FIG. 1 CONT'D

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391551 aaactccccc tcatcagttc aagcaattct tgtgcctcag cctcccgagt
391601 agctggaatt acaggtgtac accaccatgc ctagctaatc tttgtatttt
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391901 agttcaagca attcttgtgc ctcagccttc tgagtggctg agattacagg
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393201 cgttgacagt agattggaaa aagaaaatgt ggtatatata caccatggaa
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394251 aqaattttcc aqtqcataca qcaatttaaa ccaqaccaaa caaattgcta
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FIG. 1 CONT'D

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395151 tgtaagcaca tggcttccac acagacctca actaaccaga atgtatttgt
395201 ttgggctagt ttaaattgct gttatgtact ggcttttaaa tgccaccaat
395251 agggtattct acctttagat ctggcttcta ctgaccttag agctaaggaa
395301 aagagtggga aaagagtaag caatcettca gcattggcga gcaccaagat
395351 tctgacgctt ctggtgtcat tttagaagca tgaaatgagt ttgtgtcatt
395401 ctttattatg gaageegata geeagaggaa aetggaaggg etetgaatgt
395451 tggaacaatc attttaagta gcctaaacat tcttcagcat acaagctaca
395501 gcaagcttta aactactcaa aacagcaact tctaatatgc aaaatgatat
395551 ttttaattgc aaaaactttg aattaaagca tttacacata cactgaaaat
395601 tootaataga ggtttotota tttttgtaaa otgaatgggt gatgatttta
395651 tttatcagtt taagttgcta agctgtctta cgaaaaaaat ttatttatag
395701 ttaatqaqct aqtqataaaa tctaaaqqqc cttggaaaaa agtactattg
395751 tatgctaatg tgaacaaaat ccagttgtcc ctcagtatct gtgggggacc
395801 ggttccagga tctcctgcag atactaaaat ccacagatgc tcaagtccct
395851 gatagaaaat ggcatagtat ttgcacataa cctacacaca tcctcccata
395901 tactttaaat gatctccaga ttacttataa tacctaatac aatgtaaatg
395951 cttqqtaaat agttqttaac qtttattqct tqqqqaataa tqacaaqaaa
396001 aaatactcta catgttcagt acaaatgcaa tttttaatat ttgcaatttg
396051 aggctggttg aatccacaga tgtggaatcc atggatacag agagctgact
396101 ttaatagcat acattaattc ttcttctgca atgaccccag ataccaacaa
396151 tgccagggac atcataaaga atacaatcat ggtctctgcc tctgaggaac
396201 tgaaggtcta atggaaagtc agatcctaag taagtggaaa actagaatgc
396251 aaatacaact ggaataatta aggaaatgaa tgtatcatgc aagtatatgg
396301 tccatgtgac acatgttaat atgtcaaata ggaaataatt atgtgcaaac
396351 tagtgacaac tatataaaaa ttgtatataa cagaaaacaa ttacacgaaa
396401 tcccagaaac caaattctcc atattccagc agatgataaa atgtgagcct
396451 ttcctcagtg aagatcatcc agtttcctag aagaacaaag tgttcttcat
396501 agccttcttc cttttttagc aataaatgtt ccatttgagc acaaaagatt
396551 gaagggtatg acaatcttta tttctgaatc catttaattc cagaaaaaca
396601 ttcaaataag agagctctac ggtttggggt aaactttggt atacaacatt
396651 acaacttaat gtcttccatc tatgctacag caaaagcaat tcaaaaaccc
396701 tctcaaggta caaacagcca aatgttactc ttaccaattt cttacatata
396751 attctgatgg gctttttgag actgagcaaa tgctgtctca ttgagatacc
396801 aaatgtattt cccaggtcca gataagcctc taagaatcag cctcaaacat
396851 ttttaaataa aaataaaact taaaaccatt tcacccactc tatggtataa
396901 gggctgcaaa tcacaggcaa agtttcgaag atgtgctgag acactaatat
396951 gttattgccc cagctgctag aacagctgtc atccacgtct ctcttctgca
397001 aacacacagt actacaagaa tgaaagggag gccgggcgtg gtggctcaca
397051 cctgtaatcc cagcactttg ggaggccgag gcaggcggat cacgaggtca
397101 ggagatcaag accatcctgg ctaacacagc gaaaccccgt ctctactaaa
397151 aatacaaaaa aattaqccqq qcctqqtaqt qqqcqcctqt agtcccaqct
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FIG. 1 CONT'D

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397201 actctggagg ctgaggcagg agaatggcgt gagcccagga ggcacagctt
397251 gcagtgaacc gagatggtgc cactgcactc cagtttgggt gacagatcga
397301 gacttgtctc agaaaaaaaa aaaaaaagaa tgaaagggaa aggaagaatg
397351 ccctgaatgc ttgactaagg agtctgagaa tgtagccttc tcccaaagta
397401 gtttgtcatc cttcaagctg aagccacctg tacaggtgag tgaagataat
397451 acccccacct tcatttagag aacagtatga ctagtgtttt agaattctct
397501 gattgtgcct accetttgtt tcataagttt tgttcaaatt catcactaat
397551 tttagaggaa aatgtaagtt cctacaactg tcatttccca accactaata
397601 agttatttga cttgaagcac aatttgcaat aatggcctct gtaagcattt
397651 ctttagcccc atcatccaag gggctgcttt catctcattc atttcatctc
397701 gtctcacttc taacctcagc catgtgctcg aaaagcaaac gaaccaagtg
397751 gcaatagcat tagcagtgaa aaaaataaca tatctagggt tgtqcaqctg
397801 actgagatct tataaaaagta ttgcttttat aggatactgt tgttttcaaa
397851 aggaaaccag aaaagaaata tcgatgatta gaaataatgt tttttctgta
397901 agtttgttct ttgttaaacc aaacaaacag gtgtcacaaa acagaacaaa
397951 aaaaccaatg atgggtcaaa gtttaaagaa atggatagat ggctgggtga
398001 agtggctcac acctgtaatc ccagcatttt aggaggcgaa ggcaggagga
398051 tcacttgaac ccaggagttc aagaccagcc tgggcaacat ggcgagactc
398101 catttcctta aaaataaaaa gattagccag tcataatggt gtgcgcctgt
398151 agttagtccc agctactcaa gaggctgagg tgggaggatc acctgagtcc
398201 aggaggttga ggctgcagtg agccgtgttc acaccactgt attccagtct
398251 gggcaagaga gcaagatcct gtctgaaaaa gaaaaaagaa atggataaaa
398301 cataatactt cattttattt tccaaatgaa ttcaaggctg gaattggtgg
398351 gtcaaattca aatctaaata tggtttcatg aatctttctc atgtggatac
398401 cccaaaagtg atttcatcta ttagtcccca gttgtatgaa aagtatcaac
398451 tgtaccctgc aatgacctaa agccaaactg aaattccagc aatggactgg
398501 cagaaccata cactattaat tcaataaatt ttcttaggta aacaggacac
398551 agagccaaca ccaacagaaa ttacatgggg ttgggggatc tagacacata
398601 aacagatgct cacaacagtg tggctggtca qatqctgtqq aqqcaacaqa
398651 attgggaagt atgcttcagc tacctaaaga gaagcaggcg cctgcaacag
398701 tgagcactca tgccaggtaa ggctctggtg gaggaactga aagaaagtca
398751 gcatggctgc agccaaacaa ctcaggcttt atcctaagag caccaggtaa
398801 tccctgaagg gtcttaagca gggaagtggc ataaacagat gtaggtctat
398851 gaaagattac tttggctgac cacagagaca tgagacgaca aaggagtgct
398901 tagaggaagt ccagatggct atggtaagcc agaaaagaag ggattgaagc
398951 ccacactagg gaaatggaga aaattgaaca agaaggaaaa tcaagaagat
399001 tctgcaactg gctgaatggg acaaggagca ctggataagc agaaaggcag
399051 agccqaaqat cacaqqcaqa cqctqaqctt qaqtqaqaqa qaactqtqct
399101 gccactcact acagcagaaa gcacagcagg cctcaggggt gatgagtcct
399151 actatggaca tttgtgccag gtacctgtgg gatattaaag tggacaagtc
399201 ccaacagatg gatttagaaa tctgaagctc aagaaaggtc tggattggag
399251 atttggaaat ctggcatgaa atcacccagg aaaaaagcaa gtgaaataag
399301 gagagcagag taccttaaga agaactctaa gaaactccaa cgggaaaggg
399351 acagggagta ccccctagaa gggactgtga aggaagaggt agaccaggag
399401 gaaaaccagg agacagagtg tcacagagat ctggggactt gagcatcaca
399451 ggcaagaggc atgctagtgt cgaatgctgc tgagacacca aacgagggaa
399501 gggtggagaa acttccattg gatttaacaa ggagaattat cagtgacctt
399551 aacaagaaca gtttcactga ggttgtgggt ggaagaggcc aggttgcagc
399601 aggttgaggc gtatgtgaaa ggtgaagaaa aggaaaccat gagtataaac
399651 aacttgttca agaaatttca ctctgaagga aaaatgagaa atcgcatagt
399701 aatcacagaa tgtgatagag ttgcaggacg ttttctgtta acctttttaa
399751 tgtaaacatt gttagaggct tgaacatgtt tgaattaatg ggaaggagcc
399801 agtagaaaca tcaaagagga gaggatgtaa caactcaatg ggccttaaga
399851 aagtagcagg gaatgggatc tgaagcagaa gtgcaacaga agcgccgggc
399901 gcagtggctc atgcctgtaa tcccagcact ttgggaggcc gaggcaggtg
399951 gatcatctga tgtcaggagt tcgagaccgg cctggccaac atggtgaaac
400001 cccatctcta ttaaaaatac aaaaattagc tgggcatagt ggtgggtgcc
400051 tgtaatcgca gctactcagg accctgaggc aggagaatcg cttgaactcg
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FIG. 1 CONT'D

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400101 qqaqacqqaq qttqcaqtqa gccaaqatca caccactgca ctccagcctq
400151 ggcaacaaaa gcaaaattct gtctctaaat aaataaataa ataaataaat
400201 gcaagagaaa ctgtagaaag gagcaagtct tccttttctt ccttccacaa
400251 gaggaggagg aaagggtgaa tgtgaatgaa agccagttta aaggttagga
400301 atccaqatgc tqqagacata ctcattctct cattctcatt ctctcccc
400351 gctgagtctc cattttacat gcccaccggc aatgtacaac agtgctgctt
400401 tctccagtat ttactgtctt ttgtattata cccatcctag tggatgggag
400451 gtggtatete atggttttga ttggcatttg gagaccatte tettetgagg
400501 tcacctattt ttcccctatg aagaaagagt taggcttttt gctaagagta
400551 agaggggagg tagcaataaa cagtggagtg gaggccgggt gtggttgctc
400601 acgcctgtaa tcccaacatt ttgggaggcc aaggcgggag gactgcttga
400651 ggctaggtgt tcaagaccag cctgggcaac atagggagac cctgtctcta
400701 caaaaaataa aaaaattagt cgaatgtggt ggtgcgcacc tgtggtccca
400751 gctacttggg agtggggagg atcacttgag cctgggagtt tgaggctgca
400801 gtgagctatg atcacatggc acactgtact ccagactggg cgacatagtg
400851 agaccctgtc tcaaaaagaa aaaagtggag tggagcaatt gggggtaaaa
400901 tggtgaagtc tgaagcagtc accagggagg atgggaaaga gcactgagca
400951 gagaaaccta gcaggatggt aagaccaagc ccagagaaag ctggagaccg
401001 taagtottta gaggtaccca totggtotoc totgtgagot tttctacccc
401051 aggaaagaag tgtgcttttg tgtatgtgtg tgtgtgtgt tgtgtgtgtg
401101 ttttaaatgt gatctaacac acagttgact tatataatta tttcattaac
401151 tgatctcctc tactaagtct attctggcta aattcagaca acactcatca
401201 tacccctctt gtgcattctt cagcacgtac acaacatgta ctttttttt
401251 ttgagatgga gtctcactgt gtcgcccagg ctggagtgca gtggcacaat
401301 ctcggctcac tgcaacctct gcctccccag gtcaggtaat tctcgtacct
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401401 attttttgta tttttagtag agacggggtt tcaccatgtt ggccaagctg
401451 gtcttgaact cctggcctcg tgtaatctgt cgcctcaatc tcccaaaatg
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401551 aactttttgt aaaaccagag aatattttga aatgtgtccg aatgccctgc
401601 ctagattcta gactctgtga ggccccagcc tcctttccta tgcatgactt
401651 actgtttaat gtagtacaca cagaagggat atcatcatca taataaaggt
401701 cctcactttc cttcacagtt tcatctaccc cacaatgact cccaggaaaa
401751 ggagggtact gtttcagact tcccagctcc cgtatattag gtggagccaa
401801 gttcttgctg cagcatacgg gcacgcttta aaattttcaa atcattttt
401851 aaaagctaca agcttgacag ctttgggttt ttatggctac ttgttttctg
401901 aagttcacag aactttatca tttggatcac acacttaaaa aaatcacttg
401951 caaaaatctc tttaaaqatq aatatqcttc ctcttcaaqa qaaacaqact
402001 agcgggtaga agaaaaagga cccgtctaga gtattaataa atagactgat
402051 attcacacaa tggattaaat ggattaaagt ccatcccaca gatgaactgt
402101 tatattaata gaatccaaat atacagttac atcctcgacc ctgaaagcag
402151 tttaaacggg tgaaattcac ccagtgctca cttgaaatga gtactctaaa
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402251 ttccqqcatt atatactttq atgttttaat gttattaqcc cacaatacac
402301 accagtttca gaaactcagt ttttgtcctc taagggcttt tagtcctccc
402351 aaaaaaagaa tagggcaaaa gcaaggaaga tcatgaatct ggttttctaa
402401 aagcattatt acaagactgc tttataaaat tgtaatcccc agctgcagag
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402551 agcaggtagg tactttatca gaggcagaca agggaaacgt cacttattta
402601 gagttcaccg cacgcctgga taaaagtcct cactaacaaa atccctgcct
402651 ttgtggattc tgtgtcggaa agggaaacga taaagaatac ggtttgtgac
402701 agcactactc tcaggagacg aaggagagat gctaagatct tggaaaggag
402751 agagaatagg aagagtcgga ggggagatct cctctcagta aaacggcacc
402801 cacagcagtc agacttcagc tacgagcaaa atcgagtccg tgcacctcaa
402851 aaaagagagg gaggcaggga aaactttccc tcgcctctcc ccatccttcc
402901 ctcctcctcg caggagagca cattaqctga ggtgctggcg ggggccgggc
402951 cggggacccc atccttcgcc ccggacgcag cgcccqcagg gactgcccgg
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FIG. 1 CONT'D

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403001 qaqcccqaqc gagggaggcg ggaggtacag gagtaacggg gcactcccgg

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403051 cccggcctgc ggggaaggga agcaggggca gggccgaggg ggaagaggcc
403101 tccgcgagct cgaccccgcg cccacacgct acctgcgagg tcagctgctg
403151 ccgcgccgtc ccgcgggacc gcagggatct ccgaagctcc aatgggcgca
403201 qaaqtqcqaq cgagcggcgg tgcccaccgg cagcgaagag gaggagcgcc
403251 agggcgccgg gcccgccggg tcacgtggcc ccggccgcct cacgtgaccc
403301 ggtgcagcgc gcgcccggga cgctacccag ccgagcatcc cgcaccgccc
403351 eggeeegge eeeggeegaa accetgetet tegggeeeta caaccegaet
403401 tctttagaag ccgattggcc gtctcaggcc cgccccgagg ccctgccact
403451 ggagtgtccc catgaaatcc ggtggctgct gccgggactt agaggctttt
403501 gtgtctgagg aaccaggaac gcgcgaggca cgggctcctg ctctgctccc
403551 cgagatggct tggctgtggg gagggtcggc ctaccacccc agagacctag
403601 gacggaaaag cgaccgagaa acttggctcc ctgcccactc tagagcgcgt
403651 ctggcccgg ggcaccaccc aggtggtgct gcctgggagg aaaggcggcg
403701 gagctgggac tagtttgttt ttactggaga cgcgcctccc tccctccccg
403751 cccctcactt cctgattgaa agtacctgag gcaggccagg gactagggaa
403801 ggtggcagct ggacaaaggt atgaaggaag gacgagatga ggcacaggtc
403851 ctggtattgg aaagaggcag aggtacctcg gaagcatgcc atagaggtta
403901 gacgggacct aagagggcat ctggtccaac cggattcgtg ttaccagcga
403951 gtaaactgag gccaggagag ggactgctac gagctgctcc agcctatcac
404001 ctataaagac tacagtccct ttgtaaaata ccatacagct ctcggagaac
404051 tcccagttgg cgctgcagga taaaatccaa acttgttggc atagcattcc
404101 agccacttgt tcacttacct ttcccatttg agctcctagg aataaacaga
404151 aaaacatttc attttctaaa tatcaccaga taacttcact tttggtaact
404201 tgaattatta aaaaagtcct accgtccctc atctcttgcc acttccccaa
404251 cattactgga ggctctggct acaaataatt tgttttcctt gactactcaa
404301 ctttctttgg attatttact ttttctctaa gtttctttac tcctttttgc
404351 tttgttcatt cttttgtctg tatctgaaat gtcctgaatc accacctccc
404401 ccacttaaaq aaaaccaggg ccaatgatta aaaaaaaaaa aaaaggtatt
404451 aaqaaactaa tqcaataaqa qaattqaqct taqttctqta tctattctqa
404501 ggtctcgctc ctgttgcact agttcctgaa taaaatgttt ttaccacttc
404551 aactactgtt tggctctggt tttcttcaac agcctccaaa gtacacatca
404601 gtttcctact catctttcaa aatccaggtc aaatgccgcc tactcttgtc
404651 ttcccagcat cctcttccct gattttttag caattgaagt tcatccagac
404701 agtgtcagct gcaacttctt ccctgatttc cagaatacta tatatattct
404751 gatacacctc acactgccca gaaatagact gcgcatttcc tgtaaaaggt
404801 gaattgtcta ttgctgtctt ctcccttaga ttataaactc tttgaaacag
404851 gattcttctg ggtttagaac agcgcctggc atgtgataga cccttaatac
404901 tcactgaatg aagtggcttg cccaaagtag tggcagttga gtgaatttac
404951 tagaagaggc ctgttttgct caaagaaact aaaatcagtt tcttttggtt
405001 gcaacccgat caaaagaact tgtgtaaaca tgtctgagag aaaaacgagg
405051 gcatggggtg tgagcaatca aatatgtcct gagccctcac tgcttatgtg
405101 tcagatgcca tacttggagc atcttggagg attaaaagct gaatgagaca
405151 tggttgctga taaggaatgt gtagtctggt tcattattcc agtacagggt
405201 qaaaaqtatt atqatacaag gtgctaagtg aacacaaacc agggaccaca
405251 aatcagggag tcagggagaa acttcatgag aaggtcagtt ggacaggaag
405301 tagataagaa qaaagaaaaa gacattccag gagagagcaa tgtgttcaaa
405351 agtagtgaca catgaaacag tactatttgt ttaggaaaaa acaaacaggt
405401 aggtgcagtg gctcatgcct gtaatcccag gccaaggcag gcaaatcact
405451 tgaggtcaag agttcaagac cagcctggcc aactttggaa aaccctgtct
405501 ctactagaaa tacaaaaatt agccagctgt ggtggcacgt gcctgtaatc
405551 ccagctactt gagaggctga ggcacaaaaa tcacttgaac ccaggaggca
405601 gaggttgtag tgagccaaga tcgcatcact gcattccagc ctgggtgaca
405651 gagtgagact ctgtctcaaa aaaacaaaaa caagtaaccc tatattgatg
405701 ccttgatgac ttcattcaca tctaggataa aggaaaccaa attaggttaa
405751 ttttaatata cttgaaagaa tgacatattt actggtattg gtgttattta
405801 ttgtattgaa taactttcta tcaggcacat cataggctct gcatctaaaa
405851 ttggcctagg ccaggcacag tgggtcacgc ctataatccc aatgctttgg
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FIG. 1 CONT'D

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405901 gaggccaagg taggtggatt gcttgagccc aggagttcaa gaccagcctg

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405951 gacaacatag caagacgctg tccctataaa taaataagaa taaaactggc
406001 ttggactaac gcgaggtgat tttttacctt tttttccagc ctcaaaagct
406051 ttctatgatt attatgtaaa aataccaaaa ttacttgttc caaagaagat
406101 gattttttt attttttgag acagcgtctt gctctgttgc tcaagctgta
406151 ctqcagtqqc atgatcataa ctcactqcag cttcaacctc catqqqctca
406201 agtgatette ceaceteage aceteageet cetgagtage taggaceaca
406251 ggtgagggcc atcaggctgg gctaatttat attttctgtg gagacggggt
406301 ttgccatgtt ggccagcctg gtctcgaact cctgagctca agcagtttgc
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406401 tggccccaaa gaagattatt ttagagcact ccaaaccttt cctttagagc
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406501 ctccagcatg tgaaaaggga gaaccactcc acttaatgct aacacatgat
406551 tacgttggga aaagtacctg tcaagaacct aataaaatat cataaggttt
406601 gtccggacat ggtggctcac gcctgtaatc ccagcacttt gggaggccaa
406651 ggcaggtaga tcacttgagg tcaggagttt gaaaccagcc tggccaacct
406701 ggtgaaaccc tgtctctact aaaaatacaa aagttagctg ggtgtggtgg
406751 tgggcacctg taatcccagc tactcaggag gctgaggtgg gagaatcact
406801 tgaaccctgg aagcagagat tgcagtgagt cgagatcatg ccactgcact
406851 ccagcctggg caacagagta agagtccatc tcaaaaataa aataaaaata
406901 aaaaatgaat aaaattgctt ctttgtcctt tggcaggcaa aatagctttt
406951 ttatttttt atttttattt tttgacacag ggtctcgccc tgtcacccag
407001 gctggagtgc agtgtcatga tctcagctca ctgcagtctc cacgtcctgg
407051 acttaagcga ccttcccacc tcagccgccc gagtagctag gactacagat
407101 gcataccacc acacctggct acttctgttt attgtttgta gacacaggat
407151 ctcactattt tgtccaggct ggtcttgaac tcctgaaccc aacggatcct
407201 cccacctcag catcccaaag tgctgggatt acaggtgtga gccactgtac
407251 ccagcccaag agagcttctt aattatggaa tttcttcact gtccatgtca
407301 gttgatggtg aaatgtttat tttttattca ttagcagtgg tccttgttcc
407351 acctqcattt agctgtggta qcaccatggc ttattaggag gtcaccaact
407401 tctggtggga gatacgcagt ctctagtctt ctgagacata gaagttctga
407451 ctgcaattga ctatgaagca ggactggtcc tctgaatgtt aacatgcatc
407501 ttgaagactt cttagagtga ccctgggatg atgatggagg tagtaagaat
407551 attctcagat ggggcttgac tcactcattt ggaatattaa aggtgaagtt
407601 acctqqqaca aactcagtga ctttatgagg aaacaatcag agaaatacat
407651 aatagcggac aagaaccttt ctagccttgg tttcctcaaa aagttaaatt
407701 tagggggaag gccaggcacg gtggctcaca cctgtaatca taacactttg
407751 ggaggccaag gtaggcagat cacttgaggt caggagttcg aaactaggct
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407901 caggagaatt tacttgggag gctcagtcag gagaatcact tgaacccaga
407951 ggcaaaggtt gcagtgagct gagatcacgc cattgcactc aaccctgggc
408001 aacatgagca aaactccata tcaaaaaaaa attaaaattg aaaaattagg
408051 gggttaaaaa aaagaggggg actgttctag attaaaagag actaaagaaa
408101 catgaaattc aaatgcagtg catgaacctt aggtagaatc ctggttccaa
408151 ttttattttt taagagatgg gggtctcact ctgtcaccca gcctggagtg
408201 cagtggcacc atcacagccc actgcagcct caaactcctg ggctcaaaag
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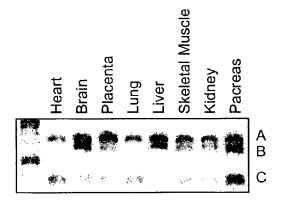
FIG. 1 CONT'D

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FIG. 1 CONT'D

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Expression of CLLD8/NY-REN-34 (ANGE) gene complex



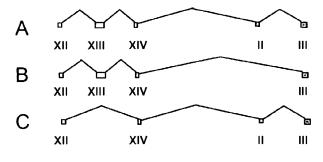


FIG. 2